UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/700,148	12/04/2000	Klaus Peter Gerbling	101215-51	2125

7590 01/13/2004

Norris McLaughlin & Marcus
30th Floor
220 East 42nd Street
New York, NY 10017

EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 01/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/700,148	GERBLING ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2003 and 05 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-27* is/are pending in the application.

4a) Of the above claim(s) *13-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This action is written in response to applicant's correspondence submitted 9/24/03 and 11/5/03. Claim 12 has been amended. Claims 12-27 are pending, and claims 13-27 are withdrawn from prosecution. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is FINAL.**

Election/Restrictions

This application contains claims 13-27 drawn to an invention nonelected with traverse in Paper No. 13. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

In the instantly rejected claims, the new limitation stating that spacers "are regions of target DNA located between the annealed fragments of (a) to (c)" in claim 12 appears to represent new matter. No specific basis for this limitation was identified in the specification, nor did a review of the specification by the examiner find any basis for the limitation. As noted in the previous office action the specification does not appear to provide a definition for this language. Since no basis has been identified, the claims are rejected as incorporating new matter.

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 12 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

New grounds of rejection are set forth to address the amended claim.

In parts (a) and (b) the use of the sequence identifier in parentheses is indefinite because it is not clear how the SEQ ID NO is meant to limit the claim. That is, it is not clear if applicant intends that the forward primer be SEQ ID NO: 15, or if its presence in parentheses means that this is one possible example of the primer but others would be acceptable. It is not clear if the presence of the SEQ ID NO indicates open (comprising) or closed (consisting of) claim language. This question is further confused by the language in the claim that recites "the forward primer, probe and reverse primer further comprising variants" because then it is not clear if applicant is stating that the primers SEQ ID NO: 15 and SEQ ID NO: 17 and probe SEQ ID NO: 16 are variants of an unnamed sequence, or if these sequences are not being claimed but

instead variants of SEQ ID NO: 15, SEQ ID NO: 16, and SEQ ID NO: 17 are being claimed. The claim does not set forth what the one, two or three nucleotide substitutions are relative to, that is what are the sequences variants of? Amendment of the claim to delete the reference ot variants and to recite, for example, "(a) a forward primer consisting of SEQ ID NO: 15" would obviate this rejection. Likewise, amendment of the claim to recite, for example, "(b) a probe consisting of SEQ ID NO: 16 wherein..." would obviate this rejection.

Claim 12 is indefinite over the recitation "spacers" throughout the claims (for example, line 5, parts (d), (e), (f), and (g). The claims are indefinite in view of this recitation because it is unclear what precisely a "spacer" is. The specification does not define this term. It is unclear if spacers are additional oligonucleotides, or if "spacers" merely represent that the forward and reverse primers would anneal to the target sequence with some unidentified stretch of intervening nucleotides between them. Clarification is requested.

Applicant's amendments to the claims are not sufficient to overcome this rejection. First, it is still not clear what the structure of the spacers (if included) would be. Are they additional oligonucleotides to be included in the kit? Is the language intended to suggest that the target sequence be included in the kit? Absent a clear definition in the specification of these additional elements it is not clear what is being claimed. Furthermore, the defintion of "spacer" which was added by amendment is indefinite itself. First, the phrase "the annealed fragments of (a) to (c)" lacks proper antecedent basis in the claims as the claim does not previously recite annealed fragments, and further, the three oligonucleotides of (a) to (c) would never be annealed to the same strand of DNA as the fragment of (c) is designed to hybridize to an opposite strand. It is further noted that there are more than 40 nucleotides between where the probe (b) would

hybridize (if the probe is SEQ ID NO: 16) and the portion of the Salmonella inv gene that is SEQ ID NO: 17.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chen *et al.* (International Journal of Food Microbiology 35(1997) 239-250) in view of all of the following: Rhan *et al.* (Molecular and Cellular Probes (1992) Vol. 6, pages 271-279), Bassler *et al.* (Applied and Environmental Microbiology, 1995, Vol. 61, No. 10, pages 3724-3728), Boyd *et al.* (Applied and Environmental Microbiology, March 1996, Vol. 62, No. 3, p. 804-808) and the Stratagene Catalog (1988).

This rejection is applied to claim 12 when claim 12 is interpreted as a claiming a kit which comprises a primer comprising or consisting of SEQ ID NO: 15, a probe comprising or consisting of SEQ ID NO: 16, and a primer that comprises or consists of the complement of SEQ ID NO: 17. These primers and probes are specific to the Salmonella invA gene.

Chen *et al.* teach a pair of primers and a probe for the amplification of the Salmonella invA gene (p. 242). Chen *et al.* teach that the target sequence amplified for the detection of Salmonella was a 287 base pair region of the invA gene as described by Rhan *et al.* (p. 242), except in their study the primer set was modified by the addition of two nucleotides on the reverse primer, and that this modification did not adversely affect the specificity of the primer (p. 247). Chen *et al.* further teach that they used a labeled probe that was designed according to the guidelines of Bassler *et al.* Chen *et al.* teach that the probe is labeled with a quencher dye that is a rhodamine derivative and a reporter dye that is a fluorescein derivative. Chen *et al.* are silent as to the precise nucleotide sequence of the primers and probe that they use.

Rhan *et al.* provide a pair of oligonucleotide primers for the amplification of a portion of the Salmonella invA gene. The primer taught by Rhan *et al.* as 139 comprises instant SEQ ID NO: 15 in its entirety. The primer taught by Rhan *et al.* differs from instant SEQ ID NO: 15 only in that it comprises an additional two nucleotides at the 3' end (Table 3 of Rhan *et al.*, p. 275). The primer taught by Rhan *et al.* as 141 is identical to the complement of SEQ ID NO: 17 except that the complement of instant SEQ ID NO: 17 has an additional two nucleotides on the 5' end (see Table 3 of Rhan *et al.*, p. 275).

Bassler *et al.* provide general guidance for the selection of probes for use in the TaqMan methods, such as those being employed by Chen *et al.* Bassler *et al.* teach that such guidelines

include "keeping the G+C content in the 40 to 60% range and avoiding extensive hairpins of self-complementary regions. Runs of identical nucleotides, especially G's and extensive regions of complementary between probe and either PCR primer should be avoided. The probe should be designed so that the predicted Tm is at least 5°C higher than the Tm of the PCR primers. Finally a G should not be the 5'-end nucleotide (p. 3725)."

Boyd *et al.* teach isolated nucleic acids which comprise the Salmonella invA gene. Boyd *et al.* disclose that the sequences of the genes are given in GenBank Accession numbers, one of these being Accession U43237 (p. 805). This GenBank record enclosed for Applicant's convenience. The sequence taught by Boyd *et al.* is a fragment which comprises instant SEQ ID NO: 15, SEQ ID NO: 16 and SEQ ID NO: 17. Specifically, instant SEQ ID NO: 15 is identical to nucleotides 269-292 of the sequence taught by Boyd *et al.*, SEQ ID NO: 16 is identical to nucleotides 333-356 of the sequence taught by Boyd *et al.*, and SEQ ID NO: 17 is identical to nucleotides 532-555 of the sequence taught by Boyd *et al.*

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have provided a pair of primers and a probe which comprise a primer consisting of SEQ ID NO: 15, a probe consisting of SEQ ID NO: 16, and a primer that consists of the complement of SEQ ID NO: 17. The ordinary practitioner would have been motivated to provide such a set by the roadmap provided by the teachings of Chen *et al.*, Rhan *et al.*, Bassler *et al.*, and Boyd *et al.* The ordinary practitioner would have been motivated to select a primer pair consisting of SEQ ID NO: 15 and the complement of SEQ ID NO: 17 because such a primer pair is only very minimally modified from the primer pair taught by Rhan *et al.* (as cited by Chen *et al.*), and Chen *et al.* specifically teach that the addition of two nucleotides to the end of the

reverse primer taught by Rhan *et al.* did not result in impairment of the ability of the primer to function. Furthermore, the ordinary practitioner would have been motivated to select any probe from within the 287 base pair amplicon amplified by such primers. Such a selection would have been motivated by the combined teachings of Chen *et al.*, Bassler *et al.*, and Boyd *et al.* Chen *et al.* specifically state that they used an oligonucleotide probe selected using the guidelines provided by Bassler *et al.*, Bassler *et al.* provide clear guidance for the selection of a probe, and Boyd *et al.* provide the entire sequence of the amplified region of the invA gene from which to select a probe. The ordinary practitioner would have been motivated to select any probe from with the 287 base pair amplified region that met the clear guidance provided by Bassler *et al.* to be provided with the primers for the detection of Salmonella. Furthermore, one would have been motivated by the teachings of Chen *et al.* to label such a probe for use in TaqMan assays, as explicitely taught by Chen *et al.*

Chen *et al.*, Rhan *et al.*, Bassler *et al.*, and Boyd *et al.* do not teach kits.

Stratagene teaches gene characterization kits.

It would have been prima facie obvious at the time the invention was made to have included the primers and probes to the Salmonella invA gene taught by Chen *et al.*, Rhan *et al.*, Bassler *et al.*, and Boyd *et al.* in a kit in order to provide a convenient way to distribute the gene to other practitioners interested in detecting the Salmonella. The ordinary practitioner would have been motivated to have produced such a kit because since the Stratagene catalog expressly teaches the benefits to the practitioner of kits:

> "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually more

> expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, pre-mixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control."

Therefore, the kits of the instant claims are *prima facie* obvious over the disclosure of Chen *et al.*, Rhan *et al.*, Bassler *et al.*, and Boyd *et al.* in view of the Stratagene catalog.

Response to Remarks

Applicant states that claim 12 has been extensively amended to comply with each basis of rejection. New grounds of rejection are set forth to address the amended claims.

Applicant argues neither Boyd nor Stratagene nor the references as described have suggested a kit employing fluorescent probes as a means to detect Salmonella contamination. However, this is not persuasive. The newly added limitation has been addressed in the pending art rejection.

Conclusion

6. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM. Please note that on January 14, 2003 the examiner's telephone number will change to (571) 272-0753.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached by calling (703) 308-1119. Beginning January 14, 2003 Gary Benzion's telephone number will be (571) 272-0782.

The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196. Beginning January 14, 2003 the receptionist's telephone number will be (571)272-0507.

JEFFREY FREDMAN
PRIMARY EXAMINER

Juliet C Switzer
Examiner
Art Unit 1634

January 7, 2004